

In the Claims

Please amend the claims as follows.

1. (Currently Amended) A first synthetic nucleic acid molecule comprising at least 300 nucleotides of a coding region for a reporter polypeptide which has at least 90% amino acid sequence identity to a reporter polypeptide encoded by a wild type nucleic acid sequence, wherein the codon composition of the first synthetic nucleic acid molecule is different at more than 25% of the codons from that of a the wild type nucleic acid sequence and is different than the codon composition of a second synthetic nucleic acid molecule which encodes a reporter polypeptide which has at least ~~85%~~ 90% amino acid sequence identity to the reporter polypeptide encoded by the wild type nucleic acid sequence, wherein the codons in the second synthetic nucleic acid molecule that are different than the codons in the wild type nucleic acid sequence are mammalian high usage codons selected to result in the second synthetic nucleic acid molecule having a reduced number of a combination of transcription factor binding sequences, intron splice sites, poly(A) addition sites and/or promoter sequences relative to the wild type nucleic acid sequence, wherein the codons which differ in the first synthetic nucleic acid molecule relative to the second synthetic nucleic acid molecule are mammalian codons selected ~~so as~~ to result in the first synthetic nucleic acid molecule having a reduced number of a ~~combination of~~ transcription factor binding sequences, ~~and~~ intron splice sites, poly(A) addition sites and/or promoter sequences, that are introduced to the second synthetic nucleic acid molecule by selecting the mammalian high usage codons relative to the wild type nucleic acid sequence, and wherein the synthetic nucleic acid molecule has reduced aberrant transcription relative to the transcription of the wild type nucleic acid sequence.

2. (Canceled).

3. (Currently Amended) The first synthetic nucleic acid molecule of claim 1 wherein the codon composition of the first synthetic nucleic acid molecule differs from the wild type nucleic acid sequence at more than 35% of the codons.

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4. (Currently Amended) The first synthetic nucleic acid molecule of claim 1 wherein the codon composition of the first synthetic nucleic acid molecule differs from the wild type nucleic acid sequence at more than 45% of the codons.
5. (Currently Amended) The first synthetic nucleic acid molecule of claim 1 wherein the codon composition of the first synthetic nucleic acid molecule differs from the wild type nucleic acid sequence at more than 55% of the codons.
6. (Currently Amended) The first synthetic nucleic acid molecule of claim 1 wherein the majority of codons which differ are ones that are preferred codons of a desired host cell.
- 7-8. (Canceled).
9. (Currently Amended) The first synthetic nucleic acid molecule of claim 1 ~~wherein the synthetic nucleic acid molecule~~ which encodes a luciferase.
10. (Canceled).
11. (Currently Amended) The first synthetic nucleic acid molecule of claim 9 wherein the wild type nucleic acid sequence encodes a beetle luciferase.
12. (Currently Amended) The first synthetic nucleic acid molecule of claim 11 wherein the first synthetic nucleic acid molecule encodes the amino acid valine at position 224.
- 13-14. (Canceled).
15. (Currently Amended) The first synthetic nucleic acid molecule of claim 1 or 9 wherein the majority of codons which differ in the second synthetic nucleic acid molecule are those which are preferred codons in humans.

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16-17. (Canceled).

18. (Currently Amended) The first synthetic nucleic acid molecule of claim 9 wherein the first synthetic nucleic acid molecule comprises SEQ ID NO:7 (GRver5), SEQ ID NO:8 (GRver6), SEQ ID NO:9 (GRver5.1), or SEQ ID NO:297 (GRver5.1).

19. (Canceled).

20. (Currently Amended) The first synthetic nucleic acid molecule of claim 15 wherein the majority of codons which differ are the human codons CGC, CTG, TCT, AGC, ACC, CCA, CCT, GCC, GGC, GTG, ATC, ATT, AAG, AAC, CAG, CAC, GAG, GAC, TAC, TGC and TTC.

21. (Currently Amended) The first synthetic nucleic acid molecule of claim 15 wherein the majority of codons which differ are the human codons CGC, CTG, TCT, ACC, CCA, GCC, GGC, GTC, and ATC or codons CGT, TTG, AGC, ACT, CCT, GCT, GGT, GTG and ATT.

22-23. (Canceled).

24. (Currently Amended) The first synthetic nucleic acid molecule of claim 1 wherein the first synthetic nucleic acid molecule is expressed in a mammalian host cell at a level which is greater than that of the wild type nucleic acid sequence.

25. (Currently Amended) The first synthetic nucleic acid molecule of claim 1 wherein the first synthetic nucleic acid molecule has an increased number of CTG or TTG leucine-encoding codons.

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26. (Currently Amended) The first synthetic nucleic acid molecule of claim 1 wherein the first synthetic nucleic acid molecule has an increased number of GTG or GTC valine-encoding codons.
27. (Currently Amended) The first synthetic nucleic acid molecule of claim 1 wherein the first synthetic nucleic acid molecule has an increased number of GGC or GGT glycine-encoding codons.
28. (Currently Amended) The first synthetic nucleic acid molecule of claim 1 wherein the first synthetic nucleic acid molecule an increased number of ATC or ATT isoleucine-encoding codons.
29. (Currently Amended) The first synthetic nucleic acid molecule of claim 1 wherein the first synthetic nucleic acid molecule has an increased number of CCA or CCT proline-encoding codons.
30. (Currently Amended) The first synthetic nucleic acid molecule of claim 1 wherein the first synthetic nucleic acid molecule has an increased number of CGC or CGT arginine-encoding codons.
31. (Currently Amended) The first synthetic nucleic acid molecule of claim 1 wherein the first synthetic nucleic acid molecule has an increased number of AGC or TCT serine-encoding codons.
32. (Currently Amended) The first synthetic nucleic acid molecule of claim 1 wherein the first synthetic nucleic acid molecule has an increased number of ACC or ACT threonine-encoding codons.

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33. (Currently Amended) The first synthetic nucleic acid molecule of claim 1 wherein the first synthetic nucleic acid molecule has an increased number of GCC or GCT alanine-encoding codons.
34. (Currently Amended) The first synthetic nucleic acid molecule of claim 1 wherein the codons in the first synthetic nucleic acid molecule which differ encode the same amino acids as the corresponding codons in the wild type nucleic acid sequence.
35. (Currently Amended) A plasmid comprising the first synthetic nucleic acid molecule of claim 1.
36. (Currently Amended) An expression vector comprising the first synthetic nucleic acid molecule of claim 1 linked to a promoter functional in a cell.
37. (Currently Amended) The expression vector of claim 36 wherein the first synthetic nucleic acid molecule is operatively linked to a Kozak consensus sequence.
38. (Original) The expression vector of claim 36 wherein the promoter is functional in a mammalian cell.
39. (Original) The expression vector of claim 36 wherein the promoter is functional in a human cell.
40. (Canceled).
41. (Original) The expression vector of claim 36 wherein the expression vector further comprises a multiple cloning site.

42. (Currently Amended) The expression vector of claim 41 wherein the expression vector comprises a multiple cloning site positioned between the promoter and the first synthetic nucleic acid molecule.
43. (Currently Amended) The expression vector of claim 41 wherein the expression vector comprises a multiple cloning site positioned downstream from the first synthetic nucleic acid molecule.
44. (Original) A host cell comprising the expression vector of claim 36.
45. (Currently Amended) A kit comprising, in suitable container means, the expression vector of claim 36, wherein the first synthetic nucleic acid molecule encodes a reporter molecule.
46. (Canceled).
47. (Currently Amended) A first polynucleotide which hybridizes under medium stringency hybridization conditions to SEQ ID NO:22 (Rluc-final), SEQ ID NO:9 (GRver5.1), SEQ ID NO:18 (RD156-1H9), SEQ ID NO:297 (GRver5.1), SEQ ID NO:301 (RD156-1H9), or the complement thereof, and comprises an open reading frame encoding a luciferase polypeptide which has at least 90% amino acid sequence identity to a luciferase encoded by a wild type nucleic acid sequence, wherein the codon composition of the open reading frame of the first polynucleotide is different at more than 25% of the codons from that of a the wild type luciferase nucleic acid sequence and is different than the codon composition of a second polynucleotide which encodes a polypeptide which has at least 85% 90% amino acid sequence identity to the polypeptide encoded by the wild type nucleic acid sequence SEQ ID NO:22, SEQ ID NO:9, SEQ ID NO:18, SEQ ID NO:297, or SEQ ID NO:301, wherein the codons in the second polynucleotide that are different than the codons in the wild type nucleic acid sequence are mammalian high usage codons selected to result in the second polynucleotide having a reduced number of a combination of transcription factor binding sequences, intron splice sites, poly(A) addition sites and/or promoter sequences relative to the wild type nucleic acid sequence, wherein

the codons which differ in the first polypeptide relative to the second polynucleotide are mammalian codons selected so as to result in the open reading frame in the first polynucleotide having a reduced number of ~~a combination of~~ transcription factor binding sequences, and intron splice sites, poly(A) addition sites and/or promoter sequences ~~relative to the wild type nucleic acid sequence~~, that are introduced to the second polynucleotide by selecting the mammalian high usage codons.

48-59. (Canceled).

60. (Currently Amended) The first synthetic nucleic acid molecule of claim 1 wherein the first synthetic nucleic acid molecule is expressed at a level which is at least 110% of that of the wild type nucleic acid sequence in a cell or cell extract under identical conditions.

61-63. (Canceled).

64. (Withdrawn) The vector of claim 63 wherein the synthetic nucleic acid molecule does not encode a polypeptide.

65-66. (Canceled).

67. (Currently Amended) A first synthetic nucleic acid molecule comprising at least 300 nucleotides of a coding region for a luciferase which has at least 90% amino acid sequence identity to a reporter polypeptide encoded by a wild type nucleic acid sequence, wherein the codon composition of the first synthetic nucleic acid molecule is different at more than 25% of the codons from that of a the wild type nucleic acid sequence and is different than the codon composition of a second synthetic nucleic acid molecule which encodes a luciferase which has at least 85% 90% amino acid sequence identity to the luciferase encoded by the wild type nucleic acid sequence, wherein the codons in the second synthetic nucleic acid molecule that are different than the codons in the wild type nucleic acid sequence are mammalian high usage codons selected to result in the second synthetic nucleic acid molecule having a reduced number

of a combination of transcription factor binding sequences, intron splice sites, poly(A) addition sites and/or promoter sequences relative to the wild type nucleic acid sequence, wherein the codons which differ in the first synthetic nucleic acid molecule relative to the second synthetic nucleic acid molecule are mammalian codons selected so as to result in a the first synthetic nucleic acid molecule having a reduced number of a combination of mammalian transcription factor binding sequences, and intron splice sites, poly(A) addition sites and/or promoter sequences, relative to the wild type nucleic acid sequence, that are introduced to the second synthetic nucleic acid molecule by selecting the mammalian high usage codons, wherein the first synthetic nucleic acid molecule has reduced aberrant transcription relative to the transcription of the wild type nucleic acid sequence, and wherein the codons which differ are codons which are employed more frequently in mammals.

68. (Canceled).

69. (Currently Amended) The first synthetic nucleic acid molecule of claim 11 or 67 which has 74% or less nucleic acid sequence identity to the wild type nucleic acid sequence.

70. (Currently Amended) The first synthetic nucleic acid molecule of claim 11 or 67 which has at least 40-fold increased expression relative to the wild type nucleic acid sequence.

71. (Currently Amended) The first polynucleotide of claim 47 which hybridizes under high stringency hybridization conditions to SEQ ID NO:22 (Rluc-final), SEQ ID NO:9 (GRver5.1), SEQ ID NO:18 (RD156-1H9), SEQ ID NO:297(GRver5.1), SEQ ID NO:301 (RD156-1H9), or the complement thereof.

72-73. (Canceled).

74. (Currently Amended) A first synthetic nucleic acid molecule comprising at least 300 nucleotides of a coding region for a luciferase which has at least 90% amino acid sequence identity to a reporter polypeptide encoded by a parent nucleic acid sequence having SEQ ID

NO:2, wherein the codon composition of the synthetic nucleic acid molecule is different at more than 25% of the codons from that of a the parent nucleic acid sequence having SEQ ID NO:2 and is different than the codon composition of a second synthetic nucleic acid molecule which encodes a luciferase which has at least 85% 90% amino acid sequence identity to the luciferase encoded by the parent nucleic acid sequence, wherein the codons in the second synthetic nucleic acid molecule that are different than the codons in the parent nucleic acid sequence are mammalian high usage codons selected to result in the second synthetic nucleic acid molecule having a reduced number of a combination of transcription factor binding sequences, intron splice sites, poly(A) addition sites and/or promoter sequences relative to the parent nucleic acid sequence, wherein the codons which differ in the first synthetic nucleic acid molecule relative to the second synthetic nucleic acid molecule are mammalian codons selected so as to result in a the first synthetic nucleic acid molecule which has reduced aberrant transcription relative to the transcription of the parent nucleic acid sequence, having a reduced number of transcription factor binding sequences, intron splice sites, poly(A) addition sites and/or promoter sequences, that are introduced to the second synthetic nucleic acid molecule by selecting the mammalian high usage codons and wherein the codons which differ are codons which are employed more frequently in mammals.

75. (Canceled).

76. (Currently Amended) The first synthetic nucleic acid molecule of claim 74 wherein the polypeptide encoded by the first synthetic nucleic acid molecule has at least 95% amino acid identity to the luciferase encoded by the parent nucleic acid sequence.

77. (Currently Amended) The first synthetic nucleic acid molecule of claim 74 which has 74% or less nucleic acid sequence identity to the parent nucleic acid sequence.

78. (Currently Amended) A first polynucleotide which hybridizes under medium stringency hybridization conditions to SEQ ID NO:9 (GRver5.1) or SEQ ID NO:297 (GRver5.1), or the complement thereof, and comprises an open reading frame encoding a luciferase polypeptide

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which has at least 90% amino acid sequence identity to a reporter polypeptide encoded by a parent nucleic acid sequence having SEQ ID NO:2, wherein the codon composition of the open reading frame of the first polynucleotide is different at more than 25% of the codons from that of a the parent luciferase nucleic acid sequence and is different than the codon composition of a second polynucleotide which encodes a polypeptide which has at least 85% 90% amino acid sequence identity to the polypeptide encoded by the parent nucleic acid sequence SEQ ID NO:9 or SEQ ID NO:297, wherein the codons in the second polynucleotide that are different than the codons in the parent nucleic acid sequence are mammalian high usage codons selected to result in the second polynucleotide having a reduced number of a combination of transcription factor binding sequences, intron splice sites, poly(A) addition sites and/or promoter sequences relative to the wild type nucleic acid sequence, wherein the codons which differ in the first polynucleotide relative to the second polynucleotide are mammalian codons selected so as to result in a the first polynucleotide which has having a reduced number of transcription factor binding sequences, intron splice sites, poly(A) addition sites and/or promoter sequences having a reduced number of transcription factor binding sequences, intron splice sites, poly(A) addition sites and/or promoter sequences that are introduced to the second polynucleotide by selecting the mammalian high usage codons reduced aberrant transcription relative to the transcription of the parent nucleic acid sequence, and wherein the codons which differ are codons which are employed more frequently in mammals.

79. (Canceled)

80. (Currently Amended) The first polynucleotide of claim 78 wherein the polypeptide encoded by the first polynucleotide has at least 95% amino acid identity to the luciferase encoded by the parent nucleic acid molecule.

81. (New) The first synthetic nucleic acid molecule of claim 1, 67 or 74 wherein the transcription factor binding sequence is at least 5 bases in length and binds a mammalian transcription factor, which binding is capable of altering transcription of downstream linked sequences.

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82. (New) The first polynucleotide of claim 47 or 78 wherein the transcription factor binding sequence is at least 5 bases in length and binds a mammalian transcription factor, which binding is capable of altering transcription of downstream linked sequences.